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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/485,640	02/11/2000	HIROYUKI ODAKA	2477US0P	2112

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EXAMINER	
JIANG, SHAOJIA A	
ART UNIT	**PAPER NUMBER**
1617	15

DATE MAILED: 05/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/485,640	Applicant(s) ODAKA ET AL.	
	Examiner Shaojia A. Jiang	Art Unit 1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 March 2003 and 07 August 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,9 and 13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,9 and 13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on March 6, 2003 has been entered in Paper No. 14.

This Office Action is a response to Applicant's request for continued examination (RCE) filed March 6, 2003 in Paper No. 14, and amendment and response to the Final Office Action (mailed March 13, 2002), filed August 7, 2002 in Paper No. 10 wherein claims 8 and 11 have been amended, and claims 2-8, 10 and 14-27 are cancelled. Currently, claims 1, 9, and 13 are pending in this application.

Claims 1, 9, and 13 are examined on the merits herein.

Applicant's amendment changing the limitation to a specific compound herein in the effective amounts in claims 1, 9, and 13 and canceling claims 2-8, 10 and 14-27 filed on August 7, 2002 in Paper No. 10 with respect to the rejection of claims 1-9 and 14 made under 35 U.S.C. 102(b) as being anticipated by Szalkowski et al. for reasons of record stated in the Office Action dated March 13, 2002, has been considered and is found persuasive to remove this particular rejection. Therefore, the said rejection is withdrawn.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Stevenson et al. (of record).

Stevenson et al. discloses that the particular thiazolidinedione, pioglitazone (5-[4-[2-(5-ethyl-2-pyridyl)ethoxy]benzyl]-2,4-thiazolidinedion) in a dose, i.e., 10 mg/kg (see x-axis for dose in Fig.2 at page 177), is anti-diabetic agent known useful in a composition to be administered to a diabetic patient (e.g. mice) and in treating diabetic complication by lowering both plasma glucose and increasing insulin sensitivity (see Introduction on page 175, and Figure 1 and the last paragraph on page 176), especially pioglitazone reducing of the elevated Tumor Necrosis Factor -α (TNF-α) mRNA levels by ~50% in mammal (see 1st paragraph of page 186). Stevenson teaches that Tumor Necrosis Factor-α (TNF-α) is known to increase insulin insensitivity (see page 185). Thus, TNF-α is tightly associated with diabetic complications. Stevenson's disclosure inherently treats Tumor Necrosis Factor-α mediated diabetic complications in a mammal such as claimed herein since Stevenson's method steps are same as the instant method steps. See *Ex parte Novitski*, 26 USPQ 2d 1389.

Thus, Stevenson et al. anticipates Claims 1 and 9.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 13 even though it is not anticipated by Stevenson et al. as applicable to claims 1 and 9, is rejected under 35 U.S.C. 103(a) as being unpatentable over the same reference by Stevenson et al. in view of Sohda et al. (WO 96/05186, PTO-892).

The same disclosure of Stevenson et al. has been discussed in the 102(b) rejection above (see supra page 3).

The prior art does not expressly disclose the employment of the particular thiazolidinedione derivative, 5-[[4-[2-(methyl-2-pyridylamino)ethoxy]phenyl]methyl]-2,4-thiazolidinedion, in a method for treating a Tumor Necrosis Factor-α mediated diabetic complications in a mammal and its effective amount.

Sohda et al. discloses that thiazolidinedione derivatives of formula (I) which has covered both pioglitazone (5-[4-[2-(5-ethyl-2-pyridyl)ethoxy]benzyl]-2,4-thiazolidinedion) and 5-[[4-[2-(methyl-2-pyridylamino)ethoxy]phenyl]methyl]-2,4-thiazolidinedion, are known antidiabetic agents and also having hypoglycemic acitivity and blood lipid lowering activity, and thus these thiazolidinedione derivatives are useful as medicines (see abstract, page 1 lines 3-7).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ the particular thiazolidinedione derivative, 5-[[4-[2-(methyl-2-pyridylamino)ethoxy]phenyl]methyl]-2,4-thiazolidinedion, in a method for treating a Tumor Necrosis Factor-α mediated diabetic complications in a mammal, and to determine its effective amounts.

One having ordinary skill in the art at the time the invention was made would have been motivated to employ the particular thiazolidinedione derivative, 5-[[4-[2-(methyl-2-pyridylamino)ethoxy]phenyl]methyl]-2,4-thiazolidinedion, in a method for treating a Tumor Necrosis Factor-α mediated diabetic complications in a mammal since thiazolidinedione derivatives of the formula I in Sohda et al. including the particular compound herein are known to be useful in compositions in treating diabetic disease and hyperglycemic diseases and hyperlipidemia. Moreover, hyperglycemic diseases and hyperlipidemia are well known diabetic complications. Therefore, one of ordinary skill in the art would have reasonably expected that the particular thiazolidinedione derivative, 5-[[4-[2-(methyl-2-pyridylamino)ethoxy]phenyl]methyl]-2,4-thiazolidinedion would exhibit their known therapeutic effect same as other derivatives of formula I such as pioglitazone in the method for treating diabetic complications, a Tumor Necrosis Factor-α mediated disease herein, absent evidence to the contrary.

Additionally, one of ordinary skill in the art would have been motivated to optimize the effective amounts of 5-[[4-[2-(methyl-2-pyridylamino)ethoxy]phenyl]methyl]-2,4-thiazolidinedion in the composition to be administered because the dose of pioglitazone to be administered is known. Therefore, the determination of another

thiazolidinedione derivative to be administered is considered well within the competence level of an ordinary skilled artisan in pharmaceutical science, involving merely routine skill in the art. It has been held that it is within the skill in the art to select optimal parameters, such as amounts of ingredients, in a composition in order to achieve a beneficial effect. See *In re Boesch*, 205 USPQ 215 (CCPA 1980).

Thus the claimed invention as a whole is clearly prima facie obvious over the combined teachings of the prior art.

Applicant's remarks filed on August 7, 2002 with respect to the rejection of claims 10, 13, and 14-27 made under 35 U.S.C. 103(a) as being unpatentable over Stevenson et al. and Szalkowski et al. of record stated in the Office Action dated March 13, 2002 have been fully considered but are moot in view of the new ground(s) of rejection above.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 9 and 13 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 6 and 12 of U.S. Patent No. 5,965,584 in view of Stevenson et al.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the patent is drawn to a method of treating diabetes in a mammal comprising administering to such a mammal a therapeutically effective amount of the insulin enhancer selected from the group consisting of pioglitazone (5-[4-[2-(5-ethyl-2-pyridyl)ethoxy]benzyl]-2,4-thiazolidinedion) and 5-[[4-[2-(methyl-2-pyridylamino)ethoxy]phenyl]methyl]-2,4-thiazolidinedion. The therapeutically effective amount of these compounds disclosed in patent is 10 mg or 30 mg for example (see Working Example 1-3 at col. 15-16), within the instant claim. The claim of the instant application is drawn to a method for treating TNF-α mediated diabetic complications in a mammal comprising administering the same compounds in the same effective amounts.

Stevenson teaches that Tumor Necrosis Factor-α (TNF-α) is known to increase insulin insensitivity (see page 185), and is thus tightly associated with diabetic complications.

One having ordinary skill in the art at the time the invention was made would have been motivated to employ the same active compounds herein in a method for treating TNF-α mediated diabetic complications in a mammal since same active compounds herein are known to be useful in a method of treating diabetes and diabetic

complications in a mammal. Therefore, one of ordinary skill in the art would have found it obvious to employ these compounds in a method for treating diabetic complications caused by TNF-α increase in a mammal.

Thus, the instant claims are seen to be obvious over the claims 6 and 12 of U.S. Patent No. 5,965,584 in view of Stevenson et al.

In view of the rejections to the pending claims set forth above, no claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Jiang, whose telephone number is (703) 305-1008. The examiner can normally be reached on Monday-Friday from 9:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, Ph.D., can be reached on (703) 305-1877. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-1235.

S. Anna Jiang, Ph.D.
Patent Examiner, AU 1617
May 6, 2003